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## Association between periodontitis and the main components of metabolic syndrome

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### Abstract

The prevalence of metabolic syndrome (MetS) is increasing worldwide, and it appears to increase independently the risk of cardiovascular disease. Periodontitis has been shown to have an association with the risk of cardiovascular disease.

The aim of the present study is to investigate the association between periodontal status and the main components of metabolic syndrome, singly, and in combination in type 2 diabetic patients.

One hundred and seventy five patients (96 males and 79 females) with type 2 diabetes mellitus (T2DM) were enrolled in the study. The following clinical characteristics were reported: age and gender, body mass index (BMI) and blood pressure. Periodontal status was assessed using periodontal disease index which includes plaque, calculus, and periodontal component of the index. An assessment of serum lipid analytes included estimation of serum triglycerides (TG) and serum high density lipoprotein cholesterol (HDL-C).

There was a significant difference in mean value of periodontal disease index (PDI) between normotensive and hypertensive diabetic patients ( $3.31 \pm 0.83$  vs.  $3.82 \pm 0.65$ ,  $P < 0.001$ ). Also there was a significant difference in PDI between normal and high TG groups ( $3.49 \pm 0.73$  vs.  $3.81 \pm 0.61$ ,  $P < 0.01$ ). There was a significant increase in TG level in hypertensive compared to normotensive diabetic patients ( $P < 0.01$ ). Only in presence of hypertension and obesity in addition to diabetes that PDI was significantly increased in comparison with diabetic hypertensive non obese patients ( $4.1 \pm 0.58$  vs.  $3.62 \pm 0.64$ ,  $P < 0.001$ ). There were no significant differences in TG level between obese and non obese diabetic patients while there was a significant increase in TG level in patients who were hypertensive obese compared to normotensive non obese ( $174.64 \pm 61.39$  vs.  $150.80 \pm 54.96$  respectively,  $P < 0.05$ ). Presence of two or more characteristics of MetS has resulted in a significant increase of PDI when compared with patients who had only diabetes ( $P < 0.001$ ).

In conclusion, hypertension and hypertriglyceridemia as main components of MetS are singly associated with periodontitis in T2DM and the presence of any two studied components of MetS in addition to diabetes will attain the worst deterioration in periodontal status.

**Key words:** Metabolic syndrome, periodontitis, hypertension, dyslipidemia, obesity

### Introduction

Metabolic syndrome (MetS) is a cluster of metabolic abnormalities that appears to be associated with an elevated risk of cardiovascular disease<sup>(1, 2)</sup>. The prevalence of this syndrome is increasing worldwide and there is an agreement that it is a major public health challenge<sup>(3)</sup>.

The definition of MetS has remained a matter of debate by several authoritative groups which have proposed the criteria to define this syndrome to be used in early clinical identification and in research purposes<sup>(4-6)</sup>. The criteria proposed by world health organization included a clinical evidence of insulin resistance, such as impaired glucose tolerance or type 2 diabetes mellitus (T2DM), as a central feature, with two or more related abnormalities (elevated blood pressure, dyslipidemia, or obesity)<sup>(4)</sup>.

Each component of MetS has been found to increase independently the risk of cardiovascular disease<sup>(7-10)</sup>. However, many studies have reported that the accumulation of these components will enhance the risk of vascular disease more significantly<sup>(11,12)</sup>.

Mild forms of periodontitis affect most adults, and more severe forms affect 5% to 20% of the population in some communities<sup>(13)</sup>. Periodontitis has been shown to have an association with the risk of cardiovascular disease<sup>(14,15)</sup> and it seems that the factors that place an individual at risk of periodontitis also place him at risk of cardiovascular disease<sup>(14-16)</sup>. These factors were mainly high blood pressure<sup>(17,18)</sup>, obesity<sup>(19)</sup> and dyslipidemia<sup>(20, 21)</sup>.

Periodontitis is more common in diabetic patients than non diabetics<sup>(22)</sup> and virtually, all patients with T2DM have some degree of insulin resistance, the central feature of MetS<sup>(23)</sup>. Moreover, the main components of MetS such as obesity, hypertension,

and plasma lipid disorders are prevalent in diabetes mellitus<sup>(24)</sup>. Therefore, the aim of study is to investigate the association between periodontal disease and the main components of metabolic syndrome, singly, and in accumulation in type 2 diabetic patients.

## Materials and Methods

This study was conducted in the National diabetes center, University of Al –Mustansiriya, Baghdad-Iraq. One hundred and seventy five patients (96 males and 79 females) with T2DM were enrolled in the study. Their ages were in the range of (31-71) years and the duration of their disease ranged from (1-25) years.

### Medical examination:

Medical history was taken by personal interviewing with the help of a printed questionnaire. All measurements were undertaken by the same examiner. Exclusion was made for those who had a concurrent acute illness or another major systemic disease except hypertension. Also patients who were taking lipid lowering agents or were smokers were excluded. The following clinical characteristics were reported:

- 1- Age and gender
- 2- Weight and height in order to calculate body mass index (BMI)
- 3- Blood pressure measurement or a history of hypertension.

### Characteristics of metabolic syndrome:

- 1- Hypertension: Blood pressure measurement higher than 140/90 or the presence of hypertension on treatment was reported as hypertensive<sup>(4)</sup>
- 2- Obesity: BMI > 30 was considered as obese<sup>(4)</sup>

- 3- Serum triglycerides level (TG): TG level  $>150$  mg/dl was considered abnormal<sup>(25)</sup>
- 4- Serum high density lipoprotein-cholesterol (HDL-C): HDL-C level  $<40$  mg/dl in males and  $<45$  in females was considered abnormal<sup>(25)</sup>

### Dental examination:

Dental measurements were undertaken by a single experienced examiner (the examiner has passed both inter- and intra-examiner calibrations). Periodontal status was assessed using periodontal disease index according to Sigurd P. and Ramfjord 1959 including plaque, calculus, and periodontal component of the index<sup>(26)</sup>.

Teeth examined: maxillary right first molar, maxillary left central, maxillary left first bicuspid, mandibular left first molar, mandibular right central, mandibular right first bicuspid. If any of the teeth are missing or unerupted, then only the teeth present are examined. The patients who were enrolled in this study had to have up to eleven teeth.

### Laboratory analyses:

#### Specimen:

Serum samples were used for lipid profile analysis that was performed on the same day of the visit of the patient.

#### Lipid profile assay:

Serum triglycerides level was determined by totally enzymatic method<sup>(27)</sup>. Estimation of serum HDL-C was done by precipitation with phosphotungstate- $MgCl_2$  solution followed by enzymatic determination of cholesterol in the supernatant<sup>(28)</sup>.

#### Statistical analysis:

Data were presented in simple statistical measures of number, percentage, mean and standard deviation. Statistical analysis was done by using Student's t- test for the significance of difference of

quantitative data between two mean values. A probability value ( $p<0.05$ ) was considered to be statistically significant.

## Results

Comparison of the means of plaque, calculus, and periodontal disease index between two groups of study patients who were classified according to the presence or absence of a certain characteristic of MetS is shown in table (1) and as follows:

1-Hypertension: The means of plaque, calculus, and periodontal disease index for normotensive and hypertensive diabetic patients were ( $1.59\pm0.49$  vs.  $1.61\pm0.58$ ,  $0.81\pm0.59$  vs.  $0.78\pm0.68$ , and  $3.31\pm0.83$  vs.  $3.82\pm0.65$  respectively). This revealed a significant difference in periodontal disease index between normotensive and hypertensive diabetic patients ( $P<0.001$ ) while no significant differences in plaque index and calculus index (Table 1).

2-Obesity: No significant differences in the means of plaque, calculus, and periodontal disease index were detected between obese and non obese diabetic patients (Table 1).

3-TG: The means of plaque, calculus, and periodontal disease index for diabetic patients with normal serum TG or high serum TG were ( $1.64\pm0.57$  vs.  $1.54\pm0.5$ ,  $0.83\pm0.67$  vs.  $0.74\pm0.60$ , and  $3.49\pm0.73$  vs.  $3.81\pm0.61$  respectively). The difference in periodontal disease index was significant ( $P<0.01$ ) while differences in plaque index and calculus index between the two groups were not significant (Table 1).

4-HDL-C: No significant differences in the means of plaque, calculus, and periodontal disease index were detected between patients with

normal HDL-C or low HDL-C level.

Analytes of dyslipidemia were compared in type 2 diabetic patients in the presence or absence of certain metabolic characteristics in table (2). There was a significant increase in TG level in hypertensive compared to normotensive diabetic patients ( $P<0.01$ ) while there was no significant difference in HDL-C level between the two groups. There were no significant differences in TG and HDL-C levels between obese and non obese diabetic patients (Table 2).

In table 3, periodontal status of type 2 diabetic patients was analyzed according to accumulation of metabolic characteristics (Diabetes plus hypertension with or without obesity and dyslipidemia). Only in the presence of hypertension and obesity in diabetics that periodontal disease index was significantly increased in comparison with diabetic hypertensive non obese patients ( $4.1\pm0.58$  vs.  $3.62\pm0.64$  respectively,  $P<0.001$ ) (Table 3).

Analytes of dyslipidemia were compared in type 2 diabetic patients according to presence of one or two metabolic characteristics (hypertension or both hypertension and obesity) (Table 4). There was a significant increase in TG level in patients who were hypertensive obese compared to normotensive non obese ( $174.64\pm61.39$  vs.  $150.80\pm54.96$  respectively,  $P<0.05$ ). There was no significant difference in HDL-C level between the two groups (Table 4).

In table 5, periodontal status of type 2 diabetic patients was analyzed in presence of two or three or four metabolic characteristics (hypertension, obesity, TG level, and HDL-C level) in addition to diabetes. Presence of two or more characteristics has resulted in a significant increase of periodontal disease index when

compared with patients who had only diabetes ( $P<0.001$ , Table 5).

## Discussion

This study has analyzed the association between components of metabolic syndrome and periodontal status in patients in whom MetS is prevalent <sup>(29)</sup>. In analyzing each component separately, hypertension was significantly associated with periodontitis. Such an association has been detected in other studies <sup>(17,18)</sup>. Some authors have attributed the association to endothelial dysfunction which is a common character of hypertension and periodontitis. Endothelial dysfunction, through a decrease in the vasodilator nitric oxide (NO) bioavailability, it decreases arterial vasodilatation. Endothelial dysfunction by itself can be attributed to the state of systemic inflammation that accompanies periodontitis <sup>(30,31)</sup>.

Dyslipidemia is a term that is commonly used to describe the presence of increased serum TG level and/or decreased serum HDL-C level <sup>(25)</sup>. Our study has detected a significant association between hypertriglyceridemia and periodontitis. Such an association has been detected in other studies <sup>(20, 21, 32, 33)</sup>.

Many investigators still raise the question of the nature between periodontitis and dyslipidemia <sup>(20,32,34)</sup> inspite of the original blaming of inflammatory response as a mediator of dyslipidemia in periodontitis <sup>(35)</sup>. In this study, serum TG level was significantly higher in hypertensive diabetic patients compared with normotensive diabetics. Such an association between hypertension and increased TG refers to a possible compound effect of hypertension and hypertriglyceridemia on periodontitis.

In this analysis, obesity by itself showed no significant association with

periodontitis but a significant association was shown if hypertension was present as well. This contradicts other reports that showed an association between obesity and periodontitis<sup>(19, 36)</sup>. Also there was no significant difference in serum TG between obese and non obese but the difference was significant in presence of hypertension. Moreover our study has detected a significant association between hypertension and hypertriglyceridemia. Thus our results may suggest a role for hypertension in mediating the bad effect of obesity on periodontitis and such a role for hypertension may even explain the association between obesity and increased TG that was reported in many studies<sup>(37)</sup>. In a recent study on the association between body weight, serum lipids and periodontitis, it was suggested that the association between body weight and periodontitis was mainly mediated through a mechanism other than serum lipids<sup>(38)</sup>.

Analysis of the combined effect of the components of MetS on periodontitis has revealed that no additive bad effect of hypertriglyceridemia on periodontal status of diabetic hypertensive obese patients was found. Moreover, an important additive deterioration in periodontal status was detected if any two studied criteria of MetS were present in addition to diabetes but no important further deterioration in periodontal status of type 2 diabetic patients was detected if a third or a fourth criterion was added. This may confirm our idea that hypertension, obesity and hypertriglyceridemia have a common pathway in their link with periodontitis.

We come to the conclusion that hypertension and hypertriglyceridemia as main components of MetS are singly associated with periodontitis in T2DM and the presence of any two studied

components of MetS in addition to diabetes will attain the worst deterioration in periodontal status.

## References

- 1- Sattar N, Gaw A, Scherbakova O, et al.: Metabolic syndrome with and without C-reactive protein as a predictor of coronary heart disease and diabetes in the West of Scotland Coronary Prevention Study. *Circulation*. 2003; 108:414-9.
- 2- Wang JJ, Li HB, Kinnunen L, et al. How well does the metabolic syndrome defined by five definitions predict incident diabetes and incident coronary heart disease in a Chinese population?. *Atherosclerosis*. 2007; 192:161-168.
- 3- Cameron AJ, Shaw JE, Zimmet PZ. The metabolic syndrome: prevalence in worldwide populations. *Endocrinol Metab Clin North Am*. 2004; 33:351-375.
- 4- Alberti KG, Zimmet PZ. Definition, diagnosis and classification of diabetes mellitus and its complications. Part1. Diagnosis and classification of diabetes mellitus provisional report of a WHO consultation. *Diabet Med*. 1998; 15:539-53.
- 5- Third Report of the National Cholesterol Education Program. (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III) final report. *Circulation*. 2002; 106: 3143- 421.
- 6- International Diabetes Federation. The IDF consensus world wide definition of the metabolic syndrome, insulin resistance, leptin resistance, and other players. *Ann. N. Y. Acad. Sci*. 2005; 892: 25-44.
- 7- McGill HC Jr, McMahan CA, Herderick EE, et al. Obesity accelerates the progression of coronary atherosclerosis in young men. *Circulation*. 2002; 105: 2712-8.
- 8- DECODE Study Group, European Diabetes Epidemiology Group. Is the current definition for diabetes relevant to mortality risk from all causes and cardiovascular and noncardiovascular diseases?. *Diabetes Care*. 2003; 26:688-696.
- 9- Eberly LE, Stamler J, Neaton JD. Multiple Risk Factor Intervention Trial Research Group. Relation of triglyceride levels, fasting and nonfasting, to fatal and nonfatal coronary heart disease. *Arch Intern Med*. 2003; 163:1077- 83.

- 10- Masley SC, Phillips SE, Schocken DD. Blood pressure as a predictor of cardiovascular events in the elderly: the William Hale Research Program. *J Hum Hypertens*. 2006; 20:392- 7.
- 11- Isomaa B, Almgren P, Tuomi T, et al. Cardiovascular morbidity and mortality associated with the metabolic syndrome. *Diabetes Care*. 2001; 24:683- 9.
- 12- Lakka HM, Laaksonen DE, Lakka TA, et al. The metabolic syndrome and total cardiovascular disease mortality in middle-aged men. *J Am Med Assoc*. 2002; 288:2709-16.
- 13- American Academy of Periodontology. Epidemiology of periodontal diseases. *J Periodontol*. 1996;67:935- 45.
- 14- Destefano F, Anda RF, Kahn HS, et al. Dental disease and risk of coronary heart disease and mortality. *Br Med J*. 1993; 306: 688- 91.
- 15- Beck JD, Offenbacher S, Williams R, et al. Periodontitis: a risk factor for coronary heart disease? *Ann of Periodontol*. 1998; 3: 127- 41.
- 16- JSHIPURA KJ, DOUGLASS CW, WILLET WC. Possible explanation for tooth loss and cardiovascular disease relationship. *Ann of Periodontol*. 1998; 3: 175- 83.
- 17- Maïborodin IV, Kolmakova IA, Pritchina IA, et al. Changes in gum in cases of arterial hypertension combination with periodontitis. *Stomatologiya (Mosk)*. 2005; 84(6):15-9.
- 18- Franek E, Klamczynska E, Ganowicz E, et al. Association of chronic periodontitis with left ventricular mass and central blood pressure in treated patients with essential hypertension. *American Journal of Hypertension*. 2009; 22 ( 2 ): 203- 7.
- 19- Saito T, Shimazaki Y, Koga T, et al. Relationship between upper body obesity and periodontitis. *J Dent Res*. 2001; 80:1631- 6.
- 20- Cutler CW, Shinedling EA, Nunn M, et al. Association between periodontitis and hyperlipidemia: cause or effect? *J Periodontol*. 1999; 70:1429-34.
- 21- Losche W, Karapetow F, Pohl A, et al. Plasma lipid and blood glucose levels in patients with destructive periodontal disease. *J Clin Periodontol*. 2000; 27: 537-41.
- 22- Soskolne WA, Klinger A. The relationship between periodontal diseases and diabetes: an overview. *Ann Periodontol*. 2001; 6: 91-8.
- 23- Kahn CR. Banting lecture : insulin action ,diabetes and the case of type 2 diabetes . *Diabetes*. 1994; 43 (8): 1066.
- 24- CDA : Canadian diabetes association. Definition,Classification and diagnosis of diabetes and other dysglycemic categories. *Canadian J diabetes*.2003; 27(Suppl2): S7-S10.
- 25- American diabetes association. Management of Dyslipidemia in Adults With diabetes .*Diabetes Care*. 2003; 26(1): S83- S86.
- 26- Peter S. Essentials of preventive and community dentistry. 2<sup>nd</sup> ed. Arya (Medi) Publishing house. New Delhi-India. 2003; p:161-6.
- 27- Fossati P, Prencipe L. Serum triglycerides determined colorimetrically with an enzyme that produces hydrogen peroxide . *Clin Chem*.1982; 28: 2077.
- 28- Assmann G, Schriewer H, Schmitz G, et al. Quantification of high density lipoprotein cholesterol by precipitation with phosphotunistic acid/ MgCl<sub>2</sub>. *Clin Chem* 1983; 29: 2026-30.
- 29- Ford ES, Giles WH, Dietz WH. Prevalence of the metabolic syndrome among US adults. Finding from The Third National Health and Nutrition Examination Survey. *JAMA*. 2002; 287: 356-9.
- 30- Amar S, Gokce N, Morgan S, et al. Periodontal disease is associated with brachial artery endothelial dysfunction and systemic inflammation. *Arterioscler Thromb Vasc Biol*. 2003; 23:1245-9.
- 31- [Higashi Y](#), [Goto C](#), [Jitsuiki D](#), et al. Periodontal infection is associated with endothelial dysfunction in healthy subjects and hypertensive patients. [Hypertension](#). 2008 ;51(2):446-53.
- 32- Cutler C W, Iacopino AM. Periodontal disease: links with serum lipid/triglyceride levels? Review and new data. *J.Int. Acad. Periodontol*. 2003; 5: 47-51.
- 33- Rufail ML, Schenkein HA, Barbour SE, et al. Altered lipoprotein subclass distribution and PAF-AH activity in subjects with generalized aggressive periodontitis. *J. Lipid Res*. 2005; 46: 2752- 60.
- 34- Iacopino A M, Cutler CW. Pathophysiological relationships between periodontitis and systemic disease: recent concepts involving serum lipids. *J. Periodontol*. 2000; 71: 1375- 84.
- 35- Memon RA, Grunfeld C, Moser AH, et al. Tumor necrosis factor mediates the effects of endotoxin on cholesterol and triglyceride metabolism in mice. *Endocrinology*. 1993; 132(5):2246-53.
- 36- Saito T, Shimazaki Y, Kiyohara Y, et al. Relationship between obesity, glucose

- tolerance, and periodontal disease in Japanese women: the Hisayama study. *J Periodontol*. 2005; 40:346- 53.
- 37- van Wijk J, Halkes C, Erkelens D, et al. Fasting and daylong triglycerides in obesity with and without type 2 diabetes. *Metabolism*. 2009; 52(8): 1043- 9.
- 38- [Saxlin T](#), [Suominen-Taipale L](#), [Kattainen A](#), et al. Association between serum lipid levels and periodontal infection. *J Clin Periodontol*. 2008; 35(12):1040-7.

Table 1: Periodontal status of type 2 diabetic patients according to the presence or absence of a metabolic characteristic

Metabolic characteristic (Total N=175)		Number (Percent %)	Plaque Index (PI) (Mean±SD)	Calculus Index (CI) (Mean±SD)	Periodontal disease Index (PDI) (Mean±SD)
Hypertension	Normotensive	71(40.6)	1.59±0.49 NS	0.81±0.59 NS	3.31±0.83 P<0.001
	Hypertensive	104(59.4)	1.61±0.58	0.78±0.68	3.82±0.65
BMI	Non Obese	98(44)	1.54±0.6 NS	0.76±0.68 NS	3.53±0.76 NS
	Obese	77(56)	1.69±0.46	0.84±0.59	3.73±0.78
TG	Normal	105(60)	1.64±0.57 NS	0.83±0.67 NS	3.49±0.73 P<0.01
	Abnormal	70(40)	1.54±0.5	0.74±0.60	3.81±0.61
HDL-C	Normal	132(24.6)	1.6±0.57 NS	0.82± 0.65 NS	3.56±0.84 NS
	Abnormal	43(75.4)	1.61±0.49	0.71±0.63	3.81±0.45

N : number

SD: standard deviation

NS: non significant

P<0.01: highly significant

Table 2: Factors of dyslipidemia in type 2 diabetic patients according to presence or absence of certain metabolic characteristics

Metabolic characteristic (Total N=175)		Number	TG (Mean±SD)	HDL-C (Mean±SD)
Hypertension	Normotensive	71(40.6)	138.32±48.21 P<0.01	44.79±2.85 NS
	Hypertensive	104(59.4)	164.85±65.15	45.15±4.34
BMI	Non Obese	98(44)	157.98±62.62 NS	44.55±4.21 NS
	Obese	77(56)	149.13±56.87	45.58±3.14

N : number

SD: standard deviation

NS: non significant

P<0.01: highly significant

Table 3: Periodontal status of type 2 diabetic patients according to accumulation of defined metabolic characteristics

Metabolic characteristic (Total N=175)		Plaque Index (PI) (Mean±SD)	Calculus Index (CI) (Mean±SD)	Periodontal disease Index (PDI) (Mean±SD)
Diabetic N=175	Normotensive N=71	1.59±0.49 NS	0.81±0.59 NS	3.31±0.83 P<0.001
	Hypertensive N=104	1.61±0.58	0.78±0.68	3.82±0.65
Diabetic+ Hypertensive N=104	Non obese N=60	1.62±0.67 NS	0.72±0.7 NS	3.62±0.64 P<0.001
	Obese N=44	1.60±0.45	0.88±0.65	4.1±0.58
Diabetic+ Hypertensive+ Obese N=44	Normal TG N=16	1.5±0.33 NS	1.04±0.66 NS	4.23±0.65 NS
	Abnormal TG N=28	1.66±0.51	0.79±0.64	4.02±0.52
	Normal HDL-C N=38	1.58±0.44 NS	0.86±0.68 NS	4.12±0.61 NS
	Abnormal HDL-C N=6	1.7±0.58	1.00± 0.52	3.97±0.34

N : number

SD: standard deviation

NS: non significant

P&lt;0.01: highly significant

Table 4: Factors of dyslipidemia in type 2 diabetic patients according to presence of one or two metabolic characteristics

Metabolic characteristic (Total N=175)		TG (Mean±SD)	HDL-C (Mean±SD)
Diabetic N=175	Normotensive N=71	138.32±48.21 P<0.01	44.79±2.85 NS
	Hypertensive N=104	164.85±65.15	45.15±4.34
Diabetic+ Hypertensive N=104	Non obese N=60	150.80±54.96 P<0.05	44.47±4.96 NS
	Obese N=44	174.64±61.39	46.09±3.12

N : number

SD: standard deviation

NS: non significant

P&lt;0.5: significant

P&lt;0.01: highly significant



Table 5: Periodontal status of type 2 diabetic patients according to presence of an additional one or more metabolic characteristic

Metabolic characteristic (Total N=175)	Plaque Index (PI) (Mean±SD)	Calculus Index (CI) (Mean±SD)	Periodontal disease Index (PDI) (Mean±SD)
Diabetic N=18	1.37±0.33	0.99±0.67	3.21±1.05
Diabetic plus one metabolic characteristic N=67	1.68±0.66 NS	0.74±0.62 NS	3.26±0.76 NS
Diabetic plus two metabolic characteristics N=46	1.55±0.49 NS	0.86±0.71 NS	4.00±0.56 P<0.001
Diabetic plus three or four metabolic characteristics N=44	1.62±0.46 P<0.05	0.73±0.58 NS	3.93±0.51 P<0.001

N : number

SD: standard deviation

P value : for comparison versus diabetic only

NS: non significant

P<0.05: significant

P<0.01: highly significant



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## Association between periodontitis and the main components of metabolic syndrome

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### Abstract

The prevalence of metabolic syndrome (MetS) is increasing worldwide, and it appears to increase independently the risk of cardiovascular disease. Periodontitis has been shown to have an association with the risk of cardiovascular disease.

The aim of the present study is to investigate the association between periodontal status and the main components of metabolic syndrome, singly, and in combination in type 2 diabetic patients.

One hundred and seventy five patients (96 males and 79 females) with type 2 diabetes mellitus (T2DM) were enrolled in the study. The following clinical characteristics were reported: age and gender, body mass index (BMI) and blood pressure. Periodontal status was assessed using periodontal disease index which includes plaque, calculus, and periodontal component of the index. An assessment of serum lipid analytes included estimation of serum triglycerides (TG) and serum high density lipoprotein cholesterol (HDL-C).

There was a significant difference in mean value of periodontal disease index (PDI) between normotensive and hypertensive diabetic patients ( $3.31 \pm 0.83$  vs.  $3.82 \pm 0.65$ ,  $P < 0.001$ ). Also there was a significant difference in PDI between normal and high TG groups ( $3.49 \pm 0.73$  vs.  $3.81 \pm 0.61$ ,  $P < 0.01$ ). There was a significant increase in TG level in hypertensive compared to normotensive diabetic patients ( $P < 0.01$ ). Only in presence of hypertension and obesity in addition to diabetes that PDI was significantly increased in comparison with diabetic hypertensive non obese patients ( $4.1 \pm 0.58$  vs.  $3.62 \pm 0.64$ ,  $P < 0.001$ ). There were no significant differences in TG level between obese and non obese diabetic patients while there was a significant increase in TG level in patients who were hypertensive obese compared to normotensive non obese ( $174.64 \pm 61.39$  vs.  $150.80 \pm 54.96$  respectively,  $P < 0.05$ ). Presence of two or more characteristics of MetS has resulted in a significant increase of PDI when compared with patients who had only diabetes ( $P < 0.001$ ).

In conclusion, hypertension and hypertriglyceridemia as main components of MetS are singly associated with periodontitis in T2DM and the presence of any two studied components of MetS in addition to diabetes will attain the worst deterioration in periodontal status.

**Key words:** Metabolic syndrome, periodontitis, hypertension, dyslipidemia, obesity

### Introduction

Metabolic syndrome (MetS) is a cluster of metabolic abnormalities that appears to be associated with an elevated risk of cardiovascular disease<sup>(1, 2)</sup>. The prevalence of this syndrome is increasing worldwide and there is an agreement that it is a major public health challenge<sup>(3)</sup>.

The definition of MetS has remained a matter of debate by several authoritative groups which have proposed the criteria to define this syndrome to be used in early clinical identification and in research purposes<sup>(4-6)</sup>. The criteria proposed by world health organization included a clinical evidence of insulin resistance, such as impaired glucose tolerance or type 2 diabetes mellitus (T2DM), as a central feature, with two or more related abnormalities (elevated blood pressure, dyslipidemia, or obesity)<sup>(4)</sup>.

Each component of MetS has been found to increase independently the risk of cardiovascular disease<sup>(7-10)</sup>. However, many studies have reported that the accumulation of these components will enhance the risk of vascular disease more significantly<sup>(11,12)</sup>.

Mild forms of periodontitis affect most adults, and more severe forms affect 5% to 20% of the population in some communities<sup>(13)</sup>. Periodontitis has been shown to have an association with the risk of cardiovascular disease<sup>(14,15)</sup> and it seems that the factors that place an individual at risk of periodontitis also place him at risk of cardiovascular disease<sup>(14-16)</sup>. These factors were mainly high blood pressure<sup>(17,18)</sup>, obesity<sup>(19)</sup> and dyslipidemia<sup>(20, 21)</sup>.

Periodontitis is more common in diabetic patients than non diabetics<sup>(22)</sup> and virtually, all patients with T2DM have some degree of insulin resistance, the central feature of MetS<sup>(23)</sup>. Moreover, the main components of MetS such as obesity, hypertension,

and plasma lipid disorders are prevalent in diabetes mellitus<sup>(24)</sup>. Therefore, the aim of study is to investigate the association between periodontal disease and the main components of metabolic syndrome, singly, and in accumulation in type 2 diabetic patients.

## Materials and Methods

This study was conducted in the National diabetes center, University of Al –Mustansiriya, Baghdad-Iraq. One hundred and seventy five patients (96 males and 79 females) with T2DM were enrolled in the study. Their ages were in the range of (31-71) years and the duration of their disease ranged from (1-25) years.

### Medical examination:

Medical history was taken by personal interviewing with the help of a printed questionnaire. All measurements were undertaken by the same examiner. Exclusion was made for those who had a concurrent acute illness or another major systemic disease except hypertension. Also patients who were taking lipid lowering agents or were smokers were excluded. The following clinical characteristics were reported:

- 1- Age and gender
- 2- Weight and height in order to calculate body mass index (BMI)
- 3- Blood pressure measurement or a history of hypertension.

### Characteristics of metabolic syndrome:

- 1- Hypertension: Blood pressure measurement higher than 140/90 or the presence of hypertension on treatment was reported as hypertensive<sup>(4)</sup>
- 2- Obesity: BMI > 30 was considered as obese<sup>(4)</sup>

- 3- Serum triglycerides level (TG): TG level  $>150$  mg/dl was considered abnormal<sup>(25)</sup>
- 4- Serum high density lipoprotein-cholesterol (HDL-C): HDL-C level  $<40$  mg/dl in males and  $<45$  in females was considered abnormal<sup>(25)</sup>

### Dental examination:

Dental measurements were undertaken by a single experienced examiner (the examiner has passed both inter- and intra-examiner calibrations). Periodontal status was assessed using periodontal disease index according to Sigurd P. and Ramfjord 1959 including plaque, calculus, and periodontal component of the index<sup>(26)</sup>.

Teeth examined: maxillary right first molar, maxillary left central, maxillary left first bicuspid, mandibular left first molar, mandibular right central, mandibular right first bicuspid. If any of the teeth are missing or unerupted, then only the teeth present are examined. The patients who were enrolled in this study had to have up to eleven teeth.

### Laboratory analyses:

#### Specimen:

Serum samples were used for lipid profile analysis that was performed on the same day of the visit of the patient.

#### Lipid profile assay:

Serum triglycerides level was determined by totally enzymatic method<sup>(27)</sup>. Estimation of serum HDL-C was done by precipitation with phosphotungstate- $MgCl_2$  solution followed by enzymatic determination of cholesterol in the supernatant<sup>(28)</sup>.

#### Statistical analysis:

Data were presented in simple statistical measures of number, percentage, mean and standard deviation. Statistical analysis was done by using Student's t- test for the significance of difference of

quantitative data between two mean values. A probability value ( $p < 0.05$ ) was considered to be statistically significant.

## Results

Comparison of the means of plaque, calculus, and periodontal disease index between two groups of study patients who were classified according to the presence or absence of a certain characteristic of MetS is shown in table (1) and as follows:

1-Hypertension: The means of plaque, calculus, and periodontal disease index for normotensive and hypertensive diabetic patients were ( $1.59 \pm 0.49$  vs.  $1.61 \pm 0.58$ ,  $0.81 \pm 0.59$  vs.  $0.78 \pm 0.68$ , and  $3.31 \pm 0.83$  vs.  $3.82 \pm 0.65$  respectively). This revealed a significant difference in periodontal disease index between normotensive and hypertensive diabetic patients ( $P < 0.001$ ) while no significant differences in plaque index and calculus index (Table 1).

2-Obesity: No significant differences in the means of plaque, calculus, and periodontal disease index were detected between obese and non obese diabetic patients (Table 1).

3-TG: The means of plaque, calculus, and periodontal disease index for diabetic patients with normal serum TG or high serum TG were ( $1.64 \pm 0.57$  vs.  $1.54 \pm 0.5$ ,  $0.83 \pm 0.67$  vs.  $0.74 \pm 0.60$ , and  $3.49 \pm 0.73$  vs.  $3.81 \pm 0.61$  respectively). The difference in periodontal disease index was significant ( $P < 0.01$ ) while differences in plaque index and calculus index between the two groups were not significant (Table 1).

4-HDL-C: No significant differences in the means of plaque, calculus, and periodontal disease index were detected between patients with

normal HDL-C or low HDL-C level.

Analytes of dyslipidemia were compared in type 2 diabetic patients in the presence or absence of certain metabolic characteristics in table (2). There was a significant increase in TG level in hypertensive compared to normotensive diabetic patients ( $P<0.01$ ) while there was no significant difference in HDL-C level between the two groups. There were no significant differences in TG and HDL-C levels between obese and non obese diabetic patients (Table 2).

In table 3, periodontal status of type 2 diabetic patients was analyzed according to accumulation of metabolic characteristics (Diabetes plus hypertension with or without obesity and dyslipidemia). Only in the presence of hypertension and obesity in diabetics that periodontal disease index was significantly increased in comparison with diabetic hypertensive non obese patients ( $4.1\pm0.58$  vs.  $3.62\pm0.64$  respectively,  $P<0.001$ ) (Table 3).

Analytes of dyslipidemia were compared in type 2 diabetic patients according to presence of one or two metabolic characteristics (hypertension or both hypertension and obesity) (Table 4). There was a significant increase in TG level in patients who were hypertensive obese compared to normotensive non obese ( $174.64\pm61.39$  vs.  $150.80\pm54.96$  respectively,  $P<0.05$ ). There was no significant difference in HDL-C level between the two groups (Table 4).

In table 5, periodontal status of type 2 diabetic patients was analyzed in presence of two or three or four metabolic characteristics (hypertension, obesity, TG level, and HDL-C level) in addition to diabetes. Presence of two or more characteristics has resulted in a significant increase of periodontal disease index when

compared with patients who had only diabetes ( $P<0.001$ , Table 5).

## Discussion

This study has analyzed the association between components of metabolic syndrome and periodontal status in patients in whom MetS is prevalent <sup>(29)</sup>. In analyzing each component separately, hypertension was significantly associated with periodontitis. Such an association has been detected in other studies <sup>(17,18)</sup>. Some authors have attributed the association to endothelial dysfunction which is a common character of hypertension and periodontitis. Endothelial dysfunction, through a decrease in the vasodilator nitric oxide (NO) bioavailability, it decreases arterial vasodilatation. Endothelial dysfunction by itself can be attributed to the state of systemic inflammation that accompanies periodontitis <sup>(30,31)</sup>.

Dyslipidemia is a term that is commonly used to describe the presence of increased serum TG level and/or decreased serum HDL-C level <sup>(25)</sup>. Our study has detected a significant association between hypertriglyceridemia and periodontitis. Such an association has been detected in other studies <sup>(20, 21, 32, 33)</sup>.

Many investigators still raise the question of the nature between periodontitis and dyslipidemia <sup>(20,32,34)</sup> inspite of the original blaming of inflammatory response as a mediator of dyslipidemia in periodontitis <sup>(35)</sup>. In this study, serum TG level was significantly higher in hypertensive diabetic patients compared with normotensive diabetics. Such an association between hypertension and increased TG refers to a possible compound effect of hypertension and hypertriglyceridemia on periodontitis.

In this analysis, obesity by itself showed no significant association with

periodontitis but a significant association was shown if hypertension was present as well. This contradicts other reports that showed an association between obesity and periodontitis<sup>(19, 36)</sup>. Also there was no significant difference in serum TG between obese and non obese but the difference was significant in presence of hypertension. Moreover our study has detected a significant association between hypertension and hypertriglyceridemia. Thus our results may suggest a role for hypertension in mediating the bad effect of obesity on periodontitis and such a role for hypertension may even explain the association between obesity and increased TG that was reported in many studies<sup>(37)</sup>. In a recent study on the association between body weight, serum lipids and periodontitis, it was suggested that the association between body weight and periodontitis was mainly mediated through a mechanism other than serum lipids<sup>(38)</sup>.

Analysis of the combined effect of the components of MetS on periodontitis has revealed that no additive bad effect of hypertriglyceridemia on periodontal status of diabetic hypertensive obese patients was found. Moreover, an important additive deterioration in periodontal status was detected if any two studied criteria of MetS were present in addition to diabetes but no important further deterioration in periodontal status of type 2 diabetic patients was detected if a third or a fourth criterion was added. This may confirm our idea that hypertension, obesity and hypertriglyceridemia have a common pathway in their link with periodontitis.

We come to the conclusion that hypertension and hypertriglyceridemia as main components of MetS are singly associated with periodontitis in T2DM and the presence of any two studied

components of MetS in addition to diabetes will attain the worst deterioration in periodontal status.

## References

- 1- Sattar N, Gaw A, Scherbakova O, et al.: Metabolic syndrome with and without C-reactive protein as a predictor of coronary heart disease and diabetes in the West of Scotland Coronary Prevention Study. *Circulation*. 2003; 108:414-9.
- 2- Wang JJ, Li HB, Kinnunen L, et al. How well does the metabolic syndrome defined by five definitions predict incident diabetes and incident coronary heart disease in a Chinese population?. *Atherosclerosis*. 2007; 192:161-168.
- 3- Cameron AJ, Shaw JE, Zimmet PZ. The metabolic syndrome: prevalence in worldwide populations. *Endocrinol Metab Clin North Am*. 2004; 33:351-375.
- 4- Alberti KG, Zimmet PZ. Definition, diagnosis and classification of diabetes mellitus and its complications. Part1. Diagnosis and classification of diabetes mellitus provisional report of a WHO consultation. *Diabet Med*. 1998; 15:539-53.
- 5- Third Report of the National Cholesterol Education Program. (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III) final report. *Circulation*. 2002; 106: 3143- 421.
- 6- International Diabetes Federation. The IDF consensus world wide definition of the metabolic syndrome, insulin resistance, leptin resistance, and other players. *Ann. N. Y. Acad. Sci*. 2005; 892: 25-44.
- 7- McGill HC Jr, McMahan CA, Herderick EE, et al. Obesity accelerates the progression of coronary atherosclerosis in young men. *Circulation*. 2002; 105: 2712-8.
- 8- DECODE Study Group, European Diabetes Epidemiology Group. Is the current definition for diabetes relevant to mortality risk from all causes and cardiovascular and noncardiovascular diseases?. *Diabetes Care*. 2003; 26:688-696.
- 9- Eberly LE, Stamler J, Neaton JD. Multiple Risk Factor Intervention Trial Research Group. Relation of triglyceride levels, fasting and nonfasting, to fatal and nonfatal coronary heart disease. *Arch Intern Med*. 2003; 163:1077- 83.

- 10- Masley SC, Phillips SE, Schocken DD. Blood pressure as a predictor of cardiovascular events in the elderly: the William Hale Research Program. *J Hum Hypertens*. 2006; 20:392- 7.
- 11- Isomaa B, Almgren P, Tuomi T, et al. Cardiovascular morbidity and mortality associated with the metabolic syndrome. *Diabetes Care*. 2001; 24:683- 9.
- 12- Lakka HM, Laaksonen DE, Lakka TA, et al. The metabolic syndrome and total cardiovascular disease mortality in middle-aged men. *J Am Med Assoc*. 2002; 288:2709-16.
- 13- American Academy of Periodontology. Epidemiology of periodontal diseases. *J Periodontol*. 1996;67:935- 45.
- 14- Destefano F, Anda RF, Kahn HS, et al. Dental disease and risk of coronary heart disease and mortality. *Br Med J*. 1993; 306: 688- 91.
- 15- Beck JD, Offenbacher S, Williams R, et al. Periodontitis: a risk factor for coronary heart disease? *Ann of Periodontol*. 1998; 3: 127- 41.
- 16- JSHIPURA KJ, DOUGLASS CW, WILLET WC. Possible explanation for tooth loss and cardiovascular disease relationship. *Ann of Periodontol*. 1998; 3: 175- 83.
- 17- Maïborodin IV, Kolmakova IA, Pritchina IA, et al. Changes in gum in cases of arterial hypertension combination with periodontitis. *Stomatologiya (Mosk)*. 2005; 84(6):15-9.
- 18- Franek E, Klamczynska E, Ganowicz E, et al. Association of chronic periodontitis with left ventricular mass and central blood pressure in treated patients with essential hypertension. *American Journal of Hypertension*. 2009; 22 ( 2 ): 203- 7.
- 19- Saito T, Shimazaki Y, Koga T, et al. Relationship between upper body obesity and periodontitis. *J Dent Res*. 2001; 80:1631- 6.
- 20- Cutler CW, Shinedling EA, Nunn M, et al. Association between periodontitis and hyperlipidemia: cause or effect? *J Periodontol*. 1999; 70:1429-34.
- 21- Losche W, Karapetow F, Pohl A, et al. Plasma lipid and blood glucose levels in patients with destructive periodontal disease. *J Clin Periodontol*. 2000; 27: 537-41.
- 22- Soskolne WA, Klinger A. The relationship between periodontal diseases and diabetes: an overview. *Ann Periodontol*. 2001; 6: 91-8.
- 23- Kahn CR. Banting lecture : insulin action ,diabetes and the case of type 2 diabetes . *Diabetes*. 1994; 43 (8): 1066.
- 24- CDA : Canadian diabetes association. Definition,Classification and diagnosis of diabetes and other dysglycemic categories. *Canadian J diabetes*.2003; 27(Suppl2): S7-S10.
- 25- American diabetes association. Management of Dyslipidemia in Adults With diabetes .*Diabetes Care*. 2003; 26(1): S83- S86.
- 26- Peter S. Essentials of preventive and community dentistry. 2<sup>nd</sup> ed. Arya (Medi) Publishing house. New Delhi-India. 2003; p:161-6.
- 27- Fossati P, Prencipe L. Serum triglycerides determined colorimetrically with an enzyme that produces hydrogen peroxide . *Clin Chem*.1982; 28: 2077.
- 28- Assmann G, Schriewer H, Schmitz G, et al. Quantification of high density lipoprotein cholesterol by precipitation with phosphotunistic acid/ MgCl<sub>2</sub>. *Clin Chem* 1983; 29: 2026-30.
- 29- Ford ES, Giles WH, Dietz WH. Prevalence of the metabolic syndrome among US adults. Finding from The Third National Health and Nutrition Examination Survey. *JAMA*. 2002; 287: 356-9.
- 30- Amar S, Gokce N, Morgan S, et al. Periodontal disease is associated with brachial artery endothelial dysfunction and systemic inflammation. *Arterioscler Thromb Vasc Biol*. 2003; 23:1245-9.
- 31- [Higashi Y](#), [Goto C](#), [Jitsuiki D](#), et al. Periodontal infection is associated with endothelial dysfunction in healthy subjects and hypertensive patients. [Hypertension](#). 2008 ;51(2):446-53.
- 32- Cutler C W, Iacopino AM. Periodontal disease: links with serum lipid/triglyceride levels? Review and new data. *J.Int. Acad. Periodontol*. 2003; 5: 47-51.
- 33- Rufail ML, Schenkein HA, Barbour SE, et al. Altered lipoprotein subclass distribution and PAF-AH activity in subjects with generalized aggressive periodontitis. *J. Lipid Res*. 2005; 46: 2752- 60.
- 34- Iacopino A M, Cutler CW. Pathophysiological relationships between periodontitis and systemic disease: recent concepts involving serum lipids. *J. Periodontol*. 2000; 71: 1375- 84.
- 35- Memon RA, Grunfeld C, Moser AH, et al. Tumor necrosis factor mediates the effects of endotoxin on cholesterol and triglyceride metabolism in mice. *Endocrinology*. 1993; 132(5):2246-53.
- 36- Saito T, Shimazaki Y, Kiyohara Y, et al. Relationship between obesity, glucose

- tolerance, and periodontal disease in Japanese women: the Hisayama study. *J Periodontol*. 2005; 40:346- 53.
- 37- van Wijk J, Halkes C, Erkelens D, et al. Fasting and daylong triglycerides in obesity with and without type 2 diabetes. *Metabolism*. 2009; 52(8): 1043- 9.
- 38- [Saxlin T](#), [Suominen-Taipale L](#), [Kattainen A](#), et al. Association between serum lipid levels and periodontal infection. *J Clin Periodontol*. 2008; 35(12):1040-7.

Table 1: Periodontal status of type 2 diabetic patients according to the presence or absence of a metabolic characteristic

Metabolic characteristic (Total N=175)		Number (Percent %)	Plaque Index (PI) (Mean±SD)	Calculus Index (CI) (Mean±SD)	Periodontal disease Index (PDI) (Mean±SD)
Hypertension	Normotensive	71(40.6)	1.59±0.49 NS	0.81±0.59 NS	3.31±0.83 P<0.001
	Hypertensive	104(59.4)	1.61±0.58	0.78±0.68	3.82±0.65
BMI	Non Obese	98(44)	1.54±0.6 NS	0.76±0.68 NS	3.53±0.76 NS
	Obese	77(56)	1.69±0.46	0.84±0.59	3.73±0.78
TG	Normal	105(60)	1.64±0.57 NS	0.83±0.67 NS	3.49±0.73 P<0.01
	Abnormal	70(40)	1.54±0.5	0.74±0.60	3.81±0.61
HDL-C	Normal	132(24.6)	1.6±0.57 NS	0.82± 0.65 NS	3.56±0.84 NS
	Abnormal	43(75.4)	1.61±0.49	0.71±0.63	3.81±0.45

N : number

SD: standard deviation

NS: non significant

P<0.01: highly significant

Table 2: Factors of dyslipidemia in type 2 diabetic patients according to presence or absence of certain metabolic characteristics

Metabolic characteristic (Total N=175)		Number	TG (Mean±SD)	HDL-C (Mean±SD)
Hypertension	Normotensive	71(40.6)	138.32±48.21 P<0.01	44.79±2.85 NS
	Hypertensive	104(59.4)	164.85±65.15	45.15±4.34
BMI	Non Obese	98(44)	157.98±62.62 NS	44.55±4.21 NS
	Obese	77(56)	149.13±56.87	45.58±3.14

N : number

SD: standard deviation

NS: non significant

P<0.01: highly significant



Table 3: Periodontal status of type 2 diabetic patients according to accumulation of defined metabolic characteristics

Metabolic characteristic (Total N=175)		Plaque Index (PI) (Mean±SD)	Calculus Index (CI) (Mean±SD)	Periodontal disease Index (PDI) (Mean±SD)
Diabetic N=175	Normotensive N=71	1.59±0.49 NS	0.81±0.59 NS	3.31±0.83 P<0.001
	Hypertensive N=104	1.61±0.58	0.78±0.68	3.82±0.65
Diabetic+ Hypertensive N=104	Non obese N=60	1.62±0.67 NS	0.72±0.7 NS	3.62±0.64 P<0.001
	Obese N=44	1.60±0.45	0.88±0.65	4.1±0.58
Diabetic+ Hypertensive+ Obese N=44	Normal TG N=16	1.5±0.33 NS	1.04±0.66 NS	4.23±0.65 NS
	Abnormal TG N=28	1.66±0.51	0.79±0.64	4.02±0.52
	Normal HDL-C N=38	1.58±0.44 NS	0.86±0.68 NS	4.12±0.61 NS
	Abnormal HDL-C N=6	1.7±0.58	1.00± 0.52	3.97±0.34

N : number

SD: standard deviation

NS: non significant

P&lt;0.01: highly significant

Table 4: Factors of dyslipidemia in type 2 diabetic patients according to presence of one or two metabolic characteristics

Metabolic characteristic (Total N=175)		TG (Mean±SD)	HDL-C (Mean±SD)
Diabetic N=175	Normotensive N=71	138.32±48.21 P<0.01	44.79±2.85 NS
	Hypertensive N=104	164.85±65.15	45.15±4.34
Diabetic+ Hypertensive N=104	Non obese N=60	150.80±54.96 P<0.05	44.47±4.96 NS
	Obese N=44	174.64±61.39	46.09±3.12

N : number

SD: standard deviation

NS: non significant

P&lt;0.5: significant

P&lt;0.01: highly significant

Table 5: Periodontal status of type 2 diabetic patients according to presence of an additional one or more metabolic characteristic

Metabolic characteristic (Total N=175)	Plaque Index (PI) (Mean±SD)	Calculus Index (CI) (Mean±SD)	Periodontal disease Index (PDI) (Mean±SD)
Diabetic N=18	1.37±0.33	0.99±0.67	3.21±1.05
Diabetic plus one metabolic characteristic N=67	1.68±0.66 NS	0.74±0.62 NS	3.26±0.76 NS
Diabetic plus two metabolic characteristics N=46	1.55±0.49 NS	0.86±0.71 NS	4.00±0.56 P<0.001
Diabetic plus three or four metabolic characteristics N=44	1.62±0.46 P<0.05	0.73±0.58 NS	3.93±0.51 P<0.001

N : number

SD: standard deviation

P value : for comparison versus diabetic only

NS: non significant

P<0.05: significant

P<0.01: highly significant